

E1
Conclude

pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, said non-hemolytic cytolytic peptide being selected from the group consisting of:

- (A) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising only D-amino acid residues, and comprising an α -helix breaker moiety;
- (B) a peptide comprising both L-amino acid residues and D-amino acid residues, having a net positive charge which is greater than +1, and having a sequence of amino acids such that a corresponding amino acid sequence comprising only L-amino acid residues is not found in nature, and cyclic derivatives thereof; and
- (C) a random copolymer consisting of a hydrophobic, a positively charged and a D-amino acid.

2 (Amended). A cyclic peptide according to claim

1 (A).

6 (Thrice-amended). A cyclic peptide according to claim 1, selected from the group of cyclic pardaxin-derived peptides consisting of the herein designated peptides 86-88 (SEQ ID NOS: 86-88, respectively), of the sequence:

86) Cyclic K¹[D]P⁷ L¹⁸L¹⁹ [1-22]-par of the sequence:

Cys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys,

87) Cyclic K¹ K²[D]P⁷ L¹⁸L¹⁹ [1-22]-par of the sequence:

Cys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys, and

88) Cyclic K¹ K²K³ [D]P⁷ L¹⁸L¹⁹ [1-22]-par of the sequence:

Cys-Lys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-
Ser-Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys.

7 (Twice-Amended). A peptide according to claim

1 (B).

9 (Amended). The peptide according to claim 8,

wherein the positively charged amino acid is selected from the group consisting of lysine, arginine and histidine, and the hydrophobic amino acid is selected from the group consisting of leucine, isoleucine, glycine, alanine, valine, phenylalanine, proline, tyrosine and tryptophan.

11 (Amended). The peptide according to claim 10,

having at least 6 amino acid residues, in which the

hydrophobic amino acid is leucine, alanine or valine, and the positively charged amino acid is lysine.

12 (Amended). The peptide according to claim 11, being a diastereomer of a 6-mer, 8-mer or 12-mer peptide composed of leucine and lysine, in which at least one third of the sequence is composed of D-amino acids, but excepting the peptide herein designated 23 (SEQ ID NO:23):

23) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂.

13 (Amended). A Leu/Lys diastereomer according to claim 12, selected from the group of peptides consisting of those herein designated 24 to 29 (SEQ ID NO:24-29, respectively), of the sequence:

24) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,

25) Lys-Lys-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Lys-Lys-NH₂,

26) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂,

27) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,

28) Lys-Leu-Leu-Leu-Leu-Lys, and

29) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys.

14 (Four Times-Amended). A cyclic derivative of a non-natural synthetic peptide according to claim 7, selected from the group of peptides consisting of those herein designated 92-95 (SEQ ID NOS 92-95, respectively), of the sequence:

92) Cyclic Cys Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys Cys,

93) Cyclic Cys Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Lys Cys,

94) HN - Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys - CO, and

95) HN - Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys - CO.

20 (Thrice-Amended). A non-hemolytic cytolytic random copolymer according to claim 1(C).

21 (Amended). The non-hemolytic cytolytic random copolymer according to claim 20, consisting of lysine, leucine and D-leucine in the ratio 1:1:1, 2:1:1 or 3:1:1 (Mol).

34 (Twice-Amended). A mixture consisting of two or more non-hemolytic cytolytic peptides or cyclic derivatives thereof, each peptide or derivative having a net positive charge which is greater than +1 and comprising both L-amino acid residues, and D-amino acid residues, or comprising only D-amino acid residues and comprising an α -helix breaker moiety.

35 (Amended). The mixture of claim 34, wherein each peptide or derivative present in the mixture consists of 12 amino acids, each of which is selected from the group consisting of L-Leu, D-Leu, L-Lys, and D-Lys

Delete claim 19 amended and insert therefor new claim 37 as follows: